REMARKS

In the Office Action mailed November 2, 2006, the Examiner objected to Claim 48, provisionally rejected Claims 34-35 and 45 on the ground of nonstatutory obviousness-type double patenting, rejected Claims 34, 35, and 45-50 under 35 U.S.C. §112(1) for failing to comply with the written description requirement, rejected Claims 46 and 50 under 35 U.S.C. §112(1) for being indefinite, rejected Claims 34, 35 and 45 under 35 U.S.C. §102(a) for being anticipated by Dennis, et al., 2001 Science 294:1102-1105 (hereinafter, "the Dennis reference"), rejected Claims 34, 35, 46 and 50 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,321,009 (hereinafter, "the '009 patent"), and rejected Claims 34, 35, 46 and 50 under 35 U.S.C. §103(a) as being obvious in light of the '009 patent. Each objection and rejection is addressed below.

I. Objection to Claim 48

The Examiner stated, "Claim 48 is objected to because of the following informalities: The phrase 'complications associated with' appears to be repeated once in error on line 2." Office Action, page 2. The Applicant now cancels Claim 48 rendering this objection moot.

II. Rejection of Claims 34, 35 and 45 under Non-Statutory Obviousness Type Double Patenting

The Examiner stated, "Claims 34-35 and 45 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10, 17 and 18 of copending Application No. 10/639,263. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are drawn to methods of treating a disease comprising administering an agent that reduces cellular ATP levels to a subject suffering from a disease comprising defective cells, wherein the agent is rapamycin and the defective cells are caused by a defective element in mTOR." Office Action, page 3.

In order to expedite prosecution while not acquiescing with the Examiner's arguments, the Applicant now submits a Terminal Disclaimer to overcome this rejection. The Applicant notes that U.S. Patent Application No. 10/639,263 has now issued as U.S. Patent No. 7,169,594. As such, the Terminal Disclaimer pertains to U.S. Patent No. 7,169,594.

III. Rejection of Claims 34, 35 and 45 under 35 U.S.C. §112(1) – Written Description

Claims 34, 35 and 45-50 were rejected under 35 U.S.C. §112(1) for lacking written description.

The Examiner stated, "Claims 34 (in lines 4 and 7) and 45 (line 1) contain the phrase, 'defective cellular energy status.' There is insufficient support for the phrase 'defective cellular energy status' in the instant specification. Accordingly, this phrase is deemed new matter." Office Action, pages 3-4. The Applicant respectfully disagrees. However, in order to expedite prosecution while not acquiescing with the Examiner's arguments, the Applicant now amends Claim 34 such that the phrase, "cells having a defective cellular energy status," is replaced with "cells having increased cellular energy, increased mTOR function, and increased phosphorylated-S6K," and Claims 42-45 are amended such that the phrase, "defective cellular energy status" is replaced with "increased mTOR function, and increased phosphorylated-S6K." Moreover, Claim 34 is amended such that the phrase, "wherein said agent reduces cellular ATP levels" is replaced with "wherein said agent is an mTOR inhibitor." Support for these amendments is located throughout the Specification (see, e.g., Figure 8H, Figure 11F, and paragraphs [0184, 0227-0230, 0239-0241, 0253-0255]).

Claim 34, as amended, does not lack written description. Support for these amendments is located throughout the Specification (see, e.g., Figure 8H, Figure 11F, and paragraphs [0184, 0227-0230, 0239-0241, 0253-0255]). One skilled in the art, upon reviewing the Specification, will recognize that cells having increased cellular energy (e.g., high levels of glucose) will have increased AKT based phosphorylation of TSC-2 which prevents TSC2 based inhibition of mTOR function, which results in increased phosphorylated-S6K. In addition, one skilled in the art, upon reviewing the Specification, will recognize that cells having decreased cellular energy (e.g., low levels of glucose) will have increased AMPK based phosphorylation of TSC-2 which permits TSC2 based inhibition of mTOR function, which results in decreased phosphorylated-S6K. It is well known in the art that diseases associated with aberrant regulation of cellular energy levels include, for example, type 2 diabetes. One skilled in the art, upon reviewing the Specification, will further recognize that subjects suffering from type 2 diabetes will have cellular energy imbalances (e.g., cells having increased cellular energy). Moreover, one skilled in the art, upon reviewing the Specification, will recognize that in cells having increased cellular energy, inhibition of mTOR function will result in decreased phosphorylated-S6K. As such, the

Specification provides adequate written description for the claimed invention, as amended. The Applicant requests the rejections be withdrawn.

IV. Rejection of Claims 46-50 under 35 U.S.C. §112(1) – Written Description

Claims 46-50 were rejected under 35 U.S.C. §112(1) for lacking written description. The Examiner stated, "Claims 46 (lines 1-2) and 50 (lines 1-2) contain the phrase 'said disease is complications associated with type 1 diabetes mellitus.' In addition, Claim 50 contains the phrase 'renal dysfunction' in line 2...Claims 47 (lines 1-2) and 49 (lines 1-2) contain the phrase 'said disease is complications associated with type 2 diabetes mellitus.' In addition, Claim 49 contains the phrase 'renal dysfunction' in line 2...Claim 48 (lines 1-2) contains the phrase 'said disease is complications associated with...metabolic syndrome'...There is insufficient support..."

The Applicant respectfully disagrees. However, in order to expedite prosecution while not acquiescing with the Examiner's arguments, the Applicant now cancels 46, 48 and 50, and amend Claim 34 such that the phrase "disease" is replaced with "type II diabetes mellitus." The Examiner is directed to, for example, Figure 8H, Figure 11F, and paragraphs [0184, 0227-0230, 0239-0241, 0253-0255] which describe the effect of cellular energy imbalance on cells. It is well known in the art that diseases associated with aberrant regulation of cellular energy levels include type II diabetes mellitus. One skilled in the art, upon reviewing the Specification, will further recognize that subjects suffering from type II diabetes mellitus (e.g., a disease preventing regulation of cellular energy levels) will have cellular energy imbalances (e.g., cells having increased cellular energy). Moreover, one skilled in the art, upon reviewing the Specification, will recognize that in cells having increased cellular energy, inhibition of mTOR function will result in decreased phosphorylated-S6K. The Applicant notes that in the August 11, 2006 Supplemental Amendment and Response, the elected group of "type I diabetes" was changed to "type II diabetes" with permission of the Examiner. As such, the Specification provides adequate written description for the claimed invention.

Regarding the term "renal dysfunction" as used in Claims 49, the Examiner is directed to, for example, Figures 13, 14, 16 and 17, and paragraphs [0186, 0251, 0253-0255, 0259 and 0260] which describes experiments conducted during the course of development of embodiments of the present invention which utilized modulated (e.g., dysfunctional) LEF cells. One skilled in the art

recognizes LEF cells as renal cells (see, e.g., Jin, et al., 1996 PNAS 93:9154-9159; attached for the Examiner's convenience). As such, the Specification provides adequate written description for the claimed invention.

V. Rejection of Claims 46-50 under 35 U.S.C. §112(2) - Indefiniteness

Claims 46-50 were rejected under 35 U.S.C. §112(2) for being indefinite. In particular, regarding Claims 46-50, the Examiner objected to the phrase, "wherein said disease is complications associated with..." type 1 diabetes mellitus, type 2 diabetes mellitus, and metabolic syndrome, and associated renal dysfunction. Claims 46, 48 and 50 are now canceled, and Claim 47 is amended such that the phrase, "wherein said disease is complications associated with..." is replaced with, "wherein said type II diabetes mellitus comprises complications associated with..." The Applicant requests these rejections be withdrawn in light of the claim amendments.

VI. Rejection of Claims 34, 35 and 45 under 35 U.S.C. §102(a)

Claims 34, 35 and 45 were rejected under 35 U.S.C. §102(a) as being anticipated by the Dennis reference. In particular, the Examiner stated, "Dennis et al teach that the mTOR pathway is influenced by the intracellular concentration of ATP and that ATP itself is an ATP sensor. Dennis et al teach that phase 1 clinical trials have shown the importance of understanding the molecular mechanisms that control mTOR function by demonstrating that rapamycin is efficacious in the treatment of solid tumors in patients with metastatic renal cell carcinoma and non-small cell lung, prostate, and breast cancer (i.e., administration of an agent to subjects wherein the agent reduces cellular ATP levels). Furthermore, Dennis et al beneficially teach that intracellular concentrations of ATP directly regulate mTOR, and that if tumors gain an mTOR-specific growth advantage because of increased production of ATP, they may be more susceptible to the effects of rapamycin (see, e.g., Abstract, pg. 1102, and pg. 1104)."

The Applicant respectfully disagrees. However, in order to expedite prosecution while not acquiescing with the Examiner's arguments, Claim 34 is now amended such that the term "disease" is replaced with "type II diabetes mellitus," the term "defective cellular energy status" is replaced with "increased cellular energy, increased mTOR function, and increased phosphorylated-S6K," and the term "said agent reduces cellular ATP levels" is replaced with,

"said agent is an mTOR inhibitor." The Dennis reference does not teach, describe, motivate and/or enable the treatment of type II diabetes mellitus, as recited in the claimed invention. The Applicant requests these rejections be withdrawn.

VII. Rejection of Claims 34, 35, 46 and 50 under 35 U.S.C. §102(b)

Claims 34, 35, 46 and 50 were rejected under 35 U.S.C. §102(b) as being anticipated by the Baeder patent. In particular, the Examiner stated, "Baeder et al teach a method of administering rapamycin to patients to prevent the onset or development and to arrest the progression of type I diabetes mellitus..." The Applicant respectfully disagrees. However, in order to expedite prosecution while not acquiescing with the Examiner's arguments, Claim 34 is now amended such that the term "disease" is replaced with "type II diabetes mellitus," the term "defective cellular energy status" is replaced with "increased cellular energy, increased mTOR function, and increased phosphorylated-S6K," and the term "said agent reduces cellular ATP levels" is replaced with, "said agent is an mTOR inhibitor." The Baeder patent does not teach, describe, motivate and/or enable the treatment of type II diabetes mellitus, as recited in the claimed invention. The Applicant requests these rejections be withdrawn.

VIII. Rejection of Claims 34, 35, 46 and 50 under 35 U.S.C. §103(a)

Claims 34, 35, 46 and 50 were rejected under 35 U.S.C. §103(a) as being obvious in light of the Baeder patent. In particular, the Examiner stated, "It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to treat a subject suffering from a disease such as diabetes type I based upon the beneficial teachings provided by Baeder et al with respect to the art-recognized method of administering rapamycin to such patients as a means of preventing the progression of β-islet cell destruction..." The Applicant respectfully disagrees. It is unclear how the Baeder patent can both anticipate and render obvious Claims 34, 35, 46 and 50. However, in order to expedite prosecution while not acquiescing with the Examiner's arguments, Claim 34 is now amended such that the term "disease" is replaced with "type II diabetes mellitus," the term "defective cellular energy status" is replaced with "increased cellular energy, increased mTOR function, and increased phosphorylated-S6K," and the term "said agent reduces cellular ATP levels" is replaced with, "said agent is an mTOR inhibitor." The Baeder patent does not teach, describe, motivate and/or enable the treatment of type II

diabetes mellitus, as recited in the claimed invention. The Applicant requests these rejections be withdrawn.

IX. Conclusion

All grounds of rejection of the Office Action of November 2, 2006 have been addressed and reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

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